TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
PCT-A0436-00		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/013982	16.09.2004	19.09.2003

International Patent Classification (IPC) or national classification and IPC

See supplemental sheet

Applicant

KISSEI PHARMACEUTICAL CO., LTD.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/013982

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/013982

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-9	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-9	NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The written opinion was formed based on documents 1 to 7 cited in the international search report:

Document 1: WO 2002/028827 A1

Document 2: JP 2003-104957 A

Document 3: WO 2003/000256 A1

Document 4: JP 2002-504110 A

Document 5: JP 8-217692 A

Document 6: JP 9-20681 A

Document 7: JP 258103 A

(1) Inventiveness of Claims 1 to 9

Documents 1 to 7

Documents 1 and 2 indicate that a 5-amidino-2-hydroxybenzenesulfonamide derivative has an activity of inhibiting activated blood coagulation factor X (hereinafter referred to as "factor Xa"), and is effective in the treatment of thromboembolisms in arteries and veins (see document 1, claims 3 to 7, 9, 11 and 12; page 28, line 16 to last line; embodiments 8, 11 and 18 to 20; document 2, paragraphs [0002] and [0051] to [0053]).

In addition, as set forth in documents 3 and 4, it would be obvious to a person skilled in the art that the

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

combined use of a factor Xa inhibiting agent and a platelet coagulation inhibitor for the treatment of thromboembolisms in arteries and veins results in an increase in the anti-thromboembolism effect, such as a reduction in the weight of thrombosis (document 3, page 1, lines 9 to 25; page 32, lines 1 to 18; page 40, line 11 to last line; document 4, claims; page 7, lines 2 to 6, page 77, line 21 to page 79, line 1; page 84, fig. 1).

It would therefore be obvious in the light of documents 3 and 4 to attempt the combined use of the factor Xa inhibiting agent and platelet coagulation inhibitor set forth in documents 1 and 2 to obtain a pharmaceutical with outstanding anti-thrombosis effect, such as reducing the weight of thrombosis.

The effect of improving the increase in coagulation of this invention of this application is examined below. As indicated in documents 5 and 6, platelets promote blood coagulation, therefore platelet coagulation inhibitors are understood to have an activity of improving increased coagulation, and document 7 indicates that aspirin has an effect of improving increased coagulation (document 5, paragraph [0005], document 6, paragraphs [0003] and [0004]; document 7, paragraphs [0049] and [0064]; page 12, fig. 7). Therefore the effect of this invention is merely due to an increase in the quantity contained of a component having an effect of improving increased coagulation, and is not a special effect.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

International Patent Classification (IPC) or national patent classification and IPC:

A61K31/216(2006.01), A61K31/4365 (2006.01) , A61K31/4709 (2006.01) , A61K31/519 (2006.01) , A61K31/616(2006.01), A61K45/00 (2006.01) , A61P7/02 (2006.01) , A61P9/04 (2006.01), A61P9/10(2006. 01), A61P43/00 (2006.01)